68 kD on a 10% SDS-PAGE gel.

92. (New) The polypeptide of Claim 85, wherein said polypeptide is recovered from a recombinant cell transformed by an isolated nucleic acid encoding said polypeptide.

93. (New) The polypeptide of Claim 85, wherein said polypeptide is of rabbit origin.

94. (New) The polypeptide of Claim 93, wherein said polypeptide has an amino acid sequence of SEQ ID NO: 12.

95. (New) An antigenic fragment of the polypeptide of Claim 85.

REMARKS

The status of the present application is that a Reply to a first Action on-the-merits has been filed and applicants are awaiting receipt of a second Action on-the-merits. With the above amendment, applicants have added eleven claims and canceled eleven claims. Accordingly, no further claim fees are required.

Applicants' invention is directed to an isolated polypeptide encoded by the LIPG gene. Prior to the present amendment, the elected claims pending in the present application defined applicants' invention in the form of a composition comprising an LIPG polypeptide. With the present amendment, applicants have added claims in the form of compound claims which define the LIPG polypeptide (Claims 85 to 95).

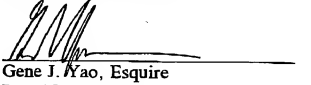
The compound claims added by the present amendment mirror the non-

elected, cancelled compound claims filed originally in parent U.S. Application No. 08/985,492 (Claims 1 to 7, 10, 32, 45, and 46; copy enclosed). In a March 30, 1999 Requirement for Restriction (copy of relevant pages thereof enclosed) issued in the `492 application, both claims defining the isolated polypeptide and claims defining a composition comprising such a polypeptide were grouped together as being drawn to the same development. Applicants note that, while the `492 application refers to the polypeptide as being an "LLG polypeptide" and the present application refers to the polypeptide as being an "LIPG polypeptide", both references are to the same polypeptide (please see pages 10 and 11 of the `492 application, copy enclosed, and the paragraph of present application which bridges pages 29 and 30). Support for Claims 85 to 95 is found in the present application at pages 25 to 28 and 35 to 37, Figure 14, Example 4, and SEQ ID NO: 12.

The non-withdrawn pending claims are Claims 20, 66 to 72, and 74 to 95.

An early and favorable action is requested respectfully.

Respectfully submitted,



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CLAIMS FROM U.S. APPLN No. 08/988,492 P.1

WE CLAIM

1. An isolated polypeptide encoded by a lipase like gene, wherein the polypeptide
(a) binds heparin,
(b) has homology with human lipoprotein lipase and hepatic lipase, and
(c) comprises a 39 kD catalytic domain of the triacylglycerol lipase family.

2. The isolated polypeptide of Claim 1, wherein 39kD catalytic domain of the triaculglycerol lipase family has the amino acid sequence of SEQ ID NO: 10.

3. The isolated polypeptide of claim 1, wherein the polypeptide has phospholipase A activity.

4. The isolated polypeptide of claim 1, wherein the polypeptide is of human origin.

5. The isolated polypeptide of claim 1, wherein the polypeptide has an amino acid sequence of SEQ ID NO:6 and an apparent molecular weight of about 40kD on a 10% SDS-PAGE gel.

6. The isolated polypeptide of claim 1, wherein the polypeptide has an amino acid sequence of SEQ ID NO:8 and an apparent molecular weight of about 55kD on a 10% SDS-PAGE gel.

7. The isolated polypeptide of claim 1, wherein the polypeptide has an amino acid sequence of SEQ ID NO:8 and an apparent molecular weight of about 68 kD on a 10% SDS-PAGE gel.

8. A composition comprising the polypeptide of claim 1 and a biologically compatible solution.

9. A pharmaceutical composition comprising the polypeptide of claim 1 and a pharmaceutically acceptable carrier.

10. An antigenic fragment of the isolated polypeptide of claim 1.

11. An isolated nucleic acid encoding the polypeptide of claim 1.

12. The isolated nucleic acid of claim 11 which is cDNA.

13. The isolated nucleic acid of claim 12, wherein the nucleotide sequence is selected from the group consisting of SEQ ID NOS: 5, 7, and 9.

14. The isolated nucleic acid of claim 13 comprising nucleotides 252-1754 of SEQ ID NO: 7.

15. An isolated nucleic acid which hybridizes at high stringency to a nucleic acid having a sequence selected from the group consisting of SEQ ID NOS: 3, 5, and 7.

16. The isolated nucleic acid of claim 15 which comprises 20 nucleotides.

17. The isolated nucleic acid of claim 15 which is an antisense nucleic acid.

18. The isolated nucleic acid of claim 17 wherein the antisense nucleic acid sequence is operably linked to a gene expression regulatory region.

19. The isolated nucleic acid of claim 15 which hybridizes at high stringency to a target selected from the group consisting of nucleotides from 44-79 of SEQ ID NO:3 and nucleotides from 1036-1065 of SEQ ID NO: 5.

20. A composition comprising the nucleic acid of claim 17 and a biologically compatible solution.

21. A pharmaceutical composition comprising the nucleic acid of claim 17 and a pharmaceutically acceptable carrier.

22. A vector comprising the isolated nucleic acid of claim 11 operable linked to a regulatory region.

23. The vector of claim 22 wherein the regulatory region is from a heterologous source.

24. The vector of claim 22 which is a viral vector.

25. The vector of claim 24 which is an adenoviral vector.

26. A recombinant cell comprising the vector of claim 22.

27. The recombinant cell of claim 26 wherein the cell is a eukaryotic cell.

28. The recombinant cell of claim 27 wherein the cell is a COS-7 cell.

29. A composition comprising the vector of claim 22 and a biologically compatible solution.

30. A pharmaceutical composition comprising the vector of claim 22 and a pharmaceutically acceptable carrier.

31. A method for preparing a polypeptide comprising culturing the recombinant cell according to claim 26 under conditions permitting the expression of the polypeptide.

32. A polypeptide prepared according to the method of claim 31.

33. An antibody capable of specifically binding to the polypeptide of claim 1.

34. An antibody of claim 33 which is able to neutralize the phospholipase activity of the polypeptide.

35. The antibody of claim 33 which is a monoclonal antibody.

36. The antibody of claim 33 which is a polyclonal antibody.

37. A hybridoma cell which produces the antibody of claim 35.

38. A composition comprising the antibody of claim 33 and a biologically compatible solution.

39. A pharmaceutical composition comprising the antibody of claim 33 and a pharmaceutically acceptable carrier.

40. A method of screening for agonists or antagonists of LLG activity comprising:

(a) contacting potential agonists of antagonists with LLG and a substrate of LLG, and

(b) measuring the ability of the potential agonists of antagonists to enhance or inhibit LLG activity, wherein the LLG is the polypeptide of claim 1.

41. A method for the enzymatic hydrolysis of a phosphatidycholine ester comprising contacting

said phosphatidycholine ester with the polypeptide of claim 1.

42. A method of improving the serum lipid profile of a human or other animal having an undesirable lipid profile comprising administration of an effective amount of the pharmaceutical composition of claim 9.

43. A method of improving the serum lipid profile of a human or other animal having a an undesirable lipid profile comprising administration of an effective amount of the pharmaceutical composition of claim 21.

44. A method of improving the serum lipid profile of a human or other animal having an undesirable lipid profile comprising administration of an effective amount of the composition of claim 39.

45. The isolated polypeptide of claim 1, wherein the polypeptide is of rabbit origin.

46. The isolated polypeptide of claim 45 which has an amino acid sequence of SEQ ID NO:12.

47. An isolated nucleic acid which encodes the polypeptide of claim 45.

48. The nucleic acid of claim 47 having a nucleic acid sequence of SEQ ID NO: 11.

49. A transgenic mouse expressing the polypeptide of claim 1.

JKB No: 08/985,492

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
08/985,492	12/05/97	JAYE	M	A2582B-US

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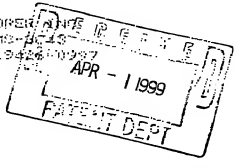
EXAMINER	
TUNG, P	

ART UNIT	PAPER NUMBER
1652	7

DATE MAILED: 03/30/99



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Commissioner of Patents and Trademarks

1 MTH Reply To OA Due - 4/30/99
2 " " " " - 5/30/99
3 " " " " - 6/30/99

P. 2 OF MARCH 30, 1999 REQUIREMENT FOR RESTRICTION ISSUED ON U.S. APPLN NO. 08/985,492

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 1-10, 32, 45 and 46, drawn to a lipase-like protein, classified in class 435, subclass 198.

II. Claims 11-16, 19, 22-29, 31, 47 and 48, drawn to DNA encoding a lipase-like protein, classified in class 536, subclass 23.2.

III. Claims 17, 18, 20 and 21, drawn to antisense DNA, classified in class 536, subclass 24.5.

IV. Claims 30 and 43, drawn to gene therapy, classified in class 514, subclass 44.

V. Claims 33-39, drawn to antibody, classified in class 530, subclass 387.9.

VI. Claim 40, drawn to a method of screening for LLG antagonists and agonists, classified in class 435, subclass 4.

VII. Claim 41, drawn to a method of hydrolyzing phosphatidyl choline ester, classified in class 435, subclass 134.

VIII. Claim 42, drawn to a method of treatment using a lipase-like protein, classified in class 424, subclass 94.1.

IX. Claim 44, drawn to a method of treatment using antibody, classified in class 424, subclass 139.1.

NH_2

Amino acids are classified into seven groups on the basis of the side chain R: (1) aliphatic side chains, (2) side chains containing a hydroxylic (OH) group, (3) side chains containing sulfur atoms, (4) side chains containing an acidic or amide group, (5) side chains containing a basic group, (6) side chains containing an aromatic ring, and (7) proline, an imino acid in which the side chain is fused to the amino group.

A **"protein"** is a polypeptide which plays a structural or functional role in a living cell. The polypeptides and proteins of the invention may be glycosylated or unglycosylated.

"Homology" means similarity of sequence reflecting a common evolutionary origin. Polypeptides or proteins are said to have homology, or similarity, if a substantial number of their amino acids are either (1) identical, or (2) have a chemically similar R side chain. Nucleic acids are said to have homology if a substantial number of their nucleotides are identical.

"Isolated polypeptide" or **"isolated protein"** is a polypeptide or protein which is substantially free of those compounds that are normally associated therewith in its natural state (e.g., other proteins or polypeptides, nucleic acids, carbohydrates, lipids). "Isolated" is not meant to exclude artificial or synthetic mixtures with other compounds, or the presence of impurities which do not interfere with biological activity, and which may be present, for example, due to incomplete purification, addition of stabilizers, or compounding into a pharmaceutically acceptable preparation.

A molecule is **"antigenic"** when it is capable of specifically interacting with an antigen recognition molecule of the immune system, such as an immunoglobulin (antibody) or T cell antigen receptor. An antigenic polypeptide contains at least about 5, and preferably at least about 10, amino acids. An antigenic portion of a molecule can be that portion that is immunodominant for antibody or T cell receptor recognition, or it can be a portion used to generate an antibody to the molecule by conjugating the antigenic portion to a carrier molecule for immunization. A molecule that is antigenic need not be itself immunogenic, *i.e.*, capable of eliciting an immune response without a carrier.

"LLGN polypeptide" and **"LLGN protein"** mean a polypeptide including the sequence SEQ ID NO: 6, said polypeptide being glycosylated or non-glycosylated.

"LLGXL polypeptide" and **"LLGXL protein"** mean a polypeptide including the sequence SEQ ID NO: 8, said polypeptide being glycosylated or non-glycosylated.

"LLG polypeptide" generically describes both the LLGN polypeptide and the LLGXL polypeptide.

The LLG polypeptide or protein of the invention includes any analogue, fragment, derivative, or mutant which is derived from an LLG polypeptide and which retains at least one biological property of the LLG polypeptide. Different variants of the LLG polypeptide exist in

nature. These variants may be allelic variations characterized by differences in the nucleotide sequences of the structural gene coding for the protein, or may involve differential splicing or post-translational modification. The skilled artisan can produce variants having single or multiple amino acid substitutions, deletions, additions, or replacements. These variants may include, inter alia: (a) variants in which one or more amino acid residues are substituted with conservative or non-conservative amino acids, (b) variants in which one or more amino acids are added to the LLG polypeptide, (c) variants in which one or more of the amino acids includes a substituent group, and (d) variants in which the LLG polypeptide is fused with another polypeptide such as serum albumin. Other LLG polypeptides of the invention include variants in which amino acid residues from one species are substituted for the corresponding residue in another species, either at conserved or non-conserved positions. In another embodiment, amino acid residues at non-conserved positions are substituted with conservative or non-conservative residues. The techniques for obtaining these variants, including genetic (suppressions, deletions, mutations, etc.), chemical, and enzymatic techniques, are known to persons having ordinary skill in the art.

If such allelic variations, analogues, fragments, derivatives, mutants, and modifications, including alternative mRNA splicing forms and alternative post-translational modification forms result in derivatives of the LLG polypeptide which retain any of the biological properties of the LLG polypeptide, they are included within the scope of this invention.

A **"nucleic acid"** is a polymeric compound comprised of covalently linked subunits called nucleotides. Nucleic acid includes polyribonucleic acid (RNA) and polydeoxyribonucleic acid (DNA), both of which may be single-stranded or double-stranded. DNA includes cDNA, genomic DNA, synthetic DNA, and semi-synthetic DNA. The sequence of nucleotides that encodes a protein is called the sense sequence.

An **"antisense nucleic acid"** is a sequence of nucleotides that is complementary to the sense sequence. Antisense nucleic acids can be used to down regulate or block the expression of the polypeptide encoded by the sense strand.

"Isolated nucleic acid" means a nucleic acid which is substantially free of those compounds that are normally associated therewith in its natural state. "Isolated" is not meant to exclude artificial or synthetic mixtures with other compounds, or the presence of impurities which do not interfere with biological activity, and which may be present, for example, due to incomplete purification, addition of stabilizers, or compounding into a pharmaceutically acceptable preparation.

The phrase **"a nucleic acid which hybridizes at high stringency"** means that the hybridized nucleic acids are able to withstand a washing under high stringency conditions. An example of high stringency washing conditions for DNA-DNA hybrids is 0.1X SSC, 0.5% SDS